

SUMMARY MINUTES
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OF THE

ORTHOPAEDICS AND REHABILITATION DEVICES

ADVISORY PANEL MEETING

OPEN SESSION

**January 12-13, 1998
Parklawn Building
5600 Fishers Lane
Rockville, MD**

**Orthopaedics and Rehabilitation Devices Panel Meeting
January 12-13, 1998**

Panel Participants

Barbara D. Boyan, Ph.D.
Chairperson (Temporary)

Albert A. Aboulafia
Consultant, deputized to vote

Marcus P. Besser, Ph.D.
Consultant, deputized to vote

Richard J. Friedman, M.D.
Consultant, deputized to vote

James A. Hill
Consultant, deputized to vote

Cato T. Laurencin, M.D., Ph.D.
Consultant, deputized to vote

Phil Lavin, Ph.D.
Consultant, deputized to vote

David L. Nelson, M.D.
Consultant, deputized to vote

Harry B. Skinner, M.D., Ph.D.
Consultant, deputized to vote

Steven H. Sterns
Consultant, deputized to vote

Michael J. Yaszemski, M.D., Ph.D.
Consultant, deputized to vote

Doris M. Holeman, Ph.D.
Consumer Representative

Raymond Silkaitis, Ph.D.
Industry Representative

FDA Participants

Jodi Nashman, M.S.
Executive Secretary
Orthopaedics and Rehabilitation Devices Advisory Panel

Celia Witten, Ph.D., M.D.
Director, Division of General and Restorative Devices (DGRD)

Jim Dillard, M.S.
Deputy Director, DGRD

Mark Melkerson, M.S.
Branch Chief
Orthopaedic Devices Branch

Capt. Marie Schroeder
Branch Chief
Restorative Devices Branch

Peter Allen, M.S.
Reviewer, Orthopaedic Devices Branch

Ken McDermott, M.S.
Reviewer, Orthopaedic Devices Branch

Ted Stevens, M.S.
Reviewer, Orthopaedic Devices Branch

Hany Demian, M.S.
Reviewer, Orthopaedic Devices Branch

Nadine Sloan, M.S.
Reviewer, Restorative Devices Branch

Orlee Panitch, M.D.
Medical Officer, DGRD

JANUARY 12, 1998--OPEN PUBLIC HEARING

Jodi Nashman, Executive Secretary, began the Open Public Hearing at 11:30 a.m. She read appointments to temporary voting status for Drs. Skinner, Yaszemski, Aboulafia, Besser, Hill, Nelson, Sterns, and Friedman. Dr. Barbara Boyan was appointed temporary chair for the January 12 sessions in the absence of a permanent panel chair. Dr. Philip Lavin was also appointed a voting member of the panel for the duration of the January 12-13, 1998 session. Ms. Nashman read the conflict of interest statement. She noted that conflict-of-interest waivers allowing full participation had been granted to Drs. Lavin, Skinner, Nelson, and Stern because of their interests in firms potentially affected by the panel's decisions; financial involvements of Drs. Boyan and Lavin that were unrelated to the agenda had been considered but deemed to pose no conflict of interest. Dr. Friedman could not participate in matters concerning shoulder reclassification because of conflict of interest considerations, but had received a waiver allowing participation in the elbow reclassification discussions. Ms. Nashman asked panel members to introduce themselves and note their areas of expertise.

Panel Chair Dr. Barbara Boyan outlined the day's agenda, which consisted of two reclassification petitions for non- and semi-constrained shoulder and elbow devices, and noted that the voting members present constituted a quorum. She invited anyone who wished to discuss those topics to address the panel. There were no requests to speak.

Mr. Mark Melkerson, M.S., Branch Chief of the Orthopedic Devices Branch, gave the branch update. After introducing branch members, he noted that the December 11-12, 1997 panel meeting had included a discussion of the minimum acceptable length of patient

follow-up for spinal implant devices and a consideration of three PMAs: the Sofamor Danek NOVUS LC, the AcroMed Brantigan I/F Cage with VSP Fixation, and the Gliatech ADCON-L. The branch was talking with these manufacturers to get each PMA to the next stage. He reviewed the subjects of the current panel meeting--four petitions proposing reclassification of preamendments and postamendments devices, as well as a proposal for classification of an unclassified preamendments device--and listed the types and categories of devices in the reclassification petitions by their current regulatory status. The Open Public Hearing was adjourned at 11:45 a.m.

OPEN SESSION

Panel Chair Dr. Barbara D. Boyan began the open session at 12:45 p.m. with the first reclassification petition.

Petition for Reclassification of Non- and Semi-Constrained Shoulder Devices

Petitioner Presentation. **Alan Wilde** and **Robert Smith** spoke on behalf of the **Orthopedic Surgical Manufacturers Association (OSMA)**, the petitioner. They noted that the FDA and a number of professional and manufacturing associations had provided input in preparing the petition. Mr. Smith listed the devices affected, noting their long history of safe use with a limited patient population, and requested that preamendment Class III metal/polymer total shoulder prostheses be reclassified as Class II devices. He listed the five separate classifications of shoulder devices: Class III total shoulders, which are constrained, semi-constrained, and non-constrained, Class II humeral hemi-shoulders, and Class III glenoid hemi-shoulders. Of these devices, the semi-constrained and non-constrained total shoulders and the humeral hemi-shoulders are the subjects of the

petition, which recommends combining semi- and non-constrained categories and reclassification of these devices into Class II and inclusion of the total and hemi (humeral)-shoulder modalities as well as the cement and cementless fixations.

Mr. Smith outlined general and device-specific risks, based on FDA classification regulations, clinical literature, and medical device reports (MDRs), saying that Class II regulatory controls are sufficient to control each of these risks. Generalized risks included component revision or loosening, gleno-humeral instability, and device failure; device-specific risks include humeral head and glenoid liner dissociation. Both kinds of risks can be controlled through elements of the 510 (k) process such as guidance documents or proof of substantial design equivalence; through manufacturing or design control regulations such as the Good Manufacturing Practices (GMP) or Quality Systems Regulations (QSR); through labeling restrictions such as indications, constraints, warnings, and precautions; and through MDRs.

On the inclusion of cementless fixation modality, Mr. Smith argued that the characteristics and limitations were well understood from other joints, that there is already extant FDA guidance, that clinical results for cementless fixation are similar to those for cemented fixation, and that the types of studies and controls associated with Class III status are not appropriate to the shoulder joint, which is of long-standing but limited use.

Mr. Smith summarized that the risks associated with non- and semi-constrained shoulder device implants have been identified and are all controllable by Class II controls and thus the device should be reclassified to Class II.

Dr. Alan Wilde discussed key review articles, saying that dislocations appear to be linked to operative technique and wear problems linked to polyethylene components now not used. He noted a low incidence of complications and device failures and a high level of pain relief, patient satisfaction, and range of motion improvement.

FDA Presentation. **Mr. Ted Stevens, M.S.**, led the FDA review of the total shoulder prostheses reclassification petition. He read the current CFR classifications for non- and semi-constrained cemented prostheses, as well as the proposed classification. He also discussed the proposed definition of the device, which he noted is fairly general, and the proposed indication for use, which does not specify any particular disease. He summarized the supporting information provided by OSMA, which consisted of review articles on cemented and uncemented fixation and a full bibliography.

Mr. Stevens summarized the device's premarket application history, noting 79 510 (k)s, of which there were 30 semi-constrained, 25 non-constrained, and 24 humeral hemis. A total of 13 companies were listed as manufacturing shoulder devices. No PMAs were cited for uncemented porous coated shoulders. He discussed MDR information, based on 102 MDRs from 1985 through 1996, all of which were for non- or semi-constrained total shoulders. He noted a discrepancy in the number of MDR reports cited by OSMA and the FDA, which he attributed to the limitations of the MDR system and problems with product coding. He listed the risks to health identified by the original classification ruling, noting that OSMA's list is more sharply delineated, as well as the special controls proposed in the petition to limit those risks.

General Panel Discussion. Panel discussion focused on whether a meta-analysis of the categories was possible and whether any one device or group was over-represented in the complications data. It was noted that a proper meta-analysis was impossible because of inconsistent reporting procedures, and that any trend in the complications data could be interpreted as a particular company having a problem and then correcting it. It was recommended that the indications for use be broadened to include rheumatoid arthritis, tumors, degenerative arthritis, and post-traumatic arthritis.

Questions and Voting. In discussion of the FDA questions, there was a clear panel consensus that the proposed definition was sufficient and that semi-constrained and non-constrained can be grouped in one classification. There was a general feeling that cemented and uncemented fixations could also be considered together, but it was noted that the mechanism of fixation for the glenoid is significantly different and deserves some recognition in review of specific devices.

Most panel members felt that the risks to health were adequately characterized, although Dr. Aboulafia drew attention to non-cemented metal-on-metal glenoid components and Dr. Boyan noted that any new information involving fixation techniques and wear results should be noted on devices reviewed. Panel members were not particularly concerned about revision of shoulders that are well fixed by biological ingrowth, whether by cemented or uncemented fixations. Panel members generally felt the information presented in the petition and in the clinical literature was sufficient to describe special controls for and to support reclassification of both humeral and glenoid biologically fixed (porous uncemented) shoulders, although there was a sense that there may be

insufficient data on uncemented glenoid components. Some panel members were inclined to recommend a patient registry as a special control, but the Industry Representative as well as some others thought it inappropriate. It was noted there are no comparable joint or animal studies outside of a clinical study that can be used to support reclassification.

The panel filled out a general device classification questionnaire and supplemental data sheet on metal/polymer shoulder prostheses, uncemented and cemented, non-constrained and semi-constrained, humeral and glenoid. These devices were not seen as life-sustaining or supporting but nonetheless of substantial importance for human health. Special controls such as performance standards and testing guidelines as specified in guidance documents and ASTM regulations and preclinical and clinical testing to ensure that biological fixation issues are being met were recommended. On the basis of the limited clinical information available, a limited postmarket survey was recommended for the uncemented glenoid fixation. The prostheses were to be used only by oral or written prescription; it was left to FDA discretion whether to restrict availability to orthopedic surgeons and operating room use only. The indications for use were those stated in the OSMA petition but should also include tumors, osteoarthritis, rheumatoid arthritis, osteonecrosis and degenerative disease, and post-traumatic arthritis. Health risks for the devices were those stated in the petition. A motion was made, seconded, and carried unanimously to accept the questionnaire and to recommend that the cemented and uncemented metal/polymer shoulder joint prosthesis, glenoid and humeral, non-constrained and semi-constrained, be recommended for reclassification as a Class II device

on the basis of the information provided in the petition and according to the standards listed, with new information on fixation and wear to be added as it becomes available.

Petition for Reclassification of Constrained Elbow Prostheses

Petitioner Presentation. **Ms. Jackie Hughes** presented the petition on behalf of **OSMA**. After noting that the petition was reviewed by the FDA and representatives of various standards groups, she stated that sufficient knowledge exists in the literature about risks associated with elbow arthroplasty and that these risks can be controlled through Class II special controls. She explained that total elbow prostheses are reconstructive devices replacing the distal humerus and the proximal ulna. Ms. Hughes reviewed the indications for use, noting that the devices serve a limited population and seek to relieve pain and improve function. At initial classification, the FDA disagreed with a panel recommendation for Class II classification because of reports of loosening and poor clinical experience with the rigid hinge, as well as limited experience with the “loose” hinge. Introduction of the Dee PMMA technique in 1972 and better understanding of the biomechanics of the elbow lead to major design revision in the late 1970s.

Ms. Hughes discussed the current status of elbow device classifications, noting that Class III constrained elbows have linkage across the joint and the Class II semi-constrained elbows have no linkage across the joint or a “loose” hinge. She contrasted differences between the regulatory definition of constrained as linkage and the medical community definition of semi-constrained as articulation with some degree of freedom. Unconstrained has no linkage, and there is no official classification for non-constrained elbows. After briefly outlining the present total elbow arthroplasty (TEA) options, she

noted that the petition seeks to address the definitions of constrained, semi-constrained, and non-constrained so that the regulatory community and medical community will have a common definition and to make miscellaneous description changes to include modularity, metal-backings, ulnar components, and titanium alloys.

Ms. Hughes discussed TEA risks outlined in the original classification regulation, which included device loosening, infection, prosthesis failure, loss or reduction of joint function, adverse tissue reaction, bone erosion, salvaging problems, and metal sensitivity , and listed special controls such as 510(k) requirements, labeling, and QSR and GMP regulations to address these risks. She also listed TEA risks in literature such as infection, ulnar nerve lesions, instability, disassembly, dislocation, subluxation, intraoperative fractures, and prosthesis failure, and listed similar controls for these risks. She discussed the review of 77 MDRs from 1985 through March 1996, including 15 for hemi-elbow classifications. Although comparisons to FDA classifications are difficult and some preamendment devices are unclassified and perhaps not captured, there were no unusual complications, and all events were similar to other orthopedic devices now in Class II.

Ms. Hughes cited support for reclassification in the literature, with 26 references supporting constrained elbow reclassification, and noted that the design concept has been in use for 20 years. She concluded that sufficient data exist on improved surgical techniques and implant designs to regulate these devices within Class II; that many of the general risks are common to other total joint prostheses successfully regulated in Class II; and that device-specific risks can be addressed with special controls.

Dr. Wilde discussed key review articles on follow-up of TEA cases. He discussed complication rates for loosening and infection, as well as overall complication and revision rates. In conclusion he recommended that “rigid” and “loose” hinged elbows be reclassified into Class II, that modularity and ulnar components be included in descriptions of semi-constrained devices, and that titanium alloys be added as an option for all elbow classifications, as suggested by the petition.

FDA Presentation. **Ken McDermott, M.S.,** reviewed the petition from the FDA perspective, describing the types of devices covered by it, their components, and the numbers cleared. He noted that the petition proposed device description changes for both Class III constrained and Class II semi-constrained devices and reclassification of the Class III device, with the main focus on the Class III device reclassification. There were no changes to the device indications. He outlined specific proposed changes to 21 CFR 888.3160 (semi-constrained) and 21 CFR 888.3150. Reclassification issues involved rigidity of the hinge, the regulatory definition of constraint (with constraint being across-the-joint linkage and semi-constrained being no across-the-joint-linkage and preventing motion in at least one plane), and metal-metal articulation as opposed to metal-polymer, which he noted might pose additional risks.

Mr. McDermott listed general risks to health, such as infection, adverse tissue reaction, loss of joint function from prosthesis loosening or dislocation, and revision due to the above, as well as specific potential risks for metal-metal articulating prostheses such as increased metal particle generation and impact of stiffness on bone remodeling. He discussed the 77 most frequently reported MDRs in the elbow classification from 1985 to

1996, citing as causes dislocation, implant fracture, and locking pin maladjustment, but noted limitations of the MDR system such as definitional problems with constraint and lack of information. In considering the supporting data cited, Mr. McDermott mentioned numerous articles regarding loose-hinged metal/polymer versions and four articles concerning the rigid-hinged version but noted there are no data cited on metal/metal articulation in this petition. He concluded by reading questions for panel discussion.

Questions and Voting. In general discussion, panel members expressed concern about metal/metal articulation, particularly involving metal bearing surfaces. It was agreed to separate metal/metal from metal/polymer devices and to consider two separate groups for reclassification issues: all elbow devices, loose or rigid hinged, with metal/polymer articulation and all elbow devices, loose or rigid hinged with metal/metal articulation. There was consensus that appropriate controls had been identified on loose or rigid hinged elbows with metal/polymer articulation but not for those with metal/metal articulation. Additional controls suggested for devices with metal/metal articulation included ASTM standards, wear testing, laboratory and animal testing, and clinical studies. Such studies could be defined for a select and special population, perhaps through the humanitarian device exemption route. There was also consensus that data presented in the petition supported reclassification of metal/polymer articulation devices but not for metal/metal, which should remain in Class III. There were no labeling changes recommended for metal/polymer articulation devices except to add an indication for use with severe degenerative changes in the elbow; metal/metal articulation devices would be covered by

Class III labeling regulatory policy. There was panel agreement that the changes to language on the semi-constrained elbow were supported by the information presented.

The panel filled out the general device classification questionnaire and supplemental data sheet for rigid and loose hinged elbow implant devices with metal/polymer articulation, saying that the device was not life-sustaining or life-supporting but was of substantial importance in preventing impairment of human health and that it did not present an unreasonable risk of illness or injury. The panel said that there was sufficient information to establish special controls and recommended normal performance standards. They restricted device use to oral or written prescription availability.

On the supplemental data sheet, the panel added an indication for use with severe degenerative changes in the elbow to those listed in the petition. The risks to health presented by the devices were listed as degeneration from wear as stated in the petition, and they listed a specific hazard to health presented by a titanium/polymer bearing surface. A motion was made, seconded, and carried unanimously to accept the worksheets as described above, thereby recommending that all elbow prostheses, loose or rigid hinged with metal/polymer articulation devices be placed in Class II on the basis of the information presented in the petition and that the existing standards identified in the petition apply to the devices, with the additional proviso that information on wear be added as it becomes available.

The panel then completed a general device classification questionnaire for rigid and loose hinged elbow devices with metal/metal articulation, in which they stated there was insufficient information to determine that general and special controls would be sufficient

for safety and effectiveness and recommending Class III classification for this device category. They suggested that the priority for requiring premarket approval application submissions for this Class III device type should be low, and availability was restricted to oral or written prescription use only. On the supplemental data sheet, the panel identified a risk to health of unknown wear debris, as well as others listed in the petition, and a specific health hazard of wear caused by the metal-on-metal or titanium-on-titanium articulation feature. The panel wanted more information before specifying further necessary restrictions on use and applicable standards. A motion was made, seconded, and carried unanimously to accept the worksheets as outlined above, thus recommending Class III for this type of device on the basis of inadequacy of clinical information available. The session was adjourned at 5:30 p.m.

JANUARY 13, 1998--OPEN PUBLIC HEARING

Executive Secretary Jodi Nashman opened the meeting at 7:30 a.m. by reading the appointments to temporary voting status for Drs. Laurencin, Yaszemski, Aboulafia, Besser, Hill, Nelson, Stern (who would be a discussant only for the knee reclassification session), Friedman (who had recused himself for the knee reclassification session), and Skinner (who would not participate in the Wright plaster of Paris pellets reclassification session). She read appointments to the temporary chair position for Dr. Boyan for the knee reclassification sessions and for Dr. Nelson for the plaster of Paris reclassification session and noted that Dr. Lavin had been appointed a temporary voting member of the panel for the duration of the January 12-13, 1998 meeting. Ms. Nashman read the conflict of interest statement, noting that because of their interests in various firms that could be

affected by the day's discussion, waivers allowing full participation had been granted to Drs. Laurencin, Nelson, Lavin, and Yaszemski. Dr. Stern could participate in all sessions but not vote on knee reclassification issues. Because of potential conflicts of interest, Dr. Friedman would not participate in the knee reclassification vote, and Drs. Boyan and Skinner would not participate in the plaster of Paris reclassification session. Ms. Nashman asked the panel to introduce themselves and note their areas of expertise.

Temporary Chair Dr. Barbara Boyan noted that the panel was to consider recommendations to the FDA on two reclassification petition and one reclassification proposal and that the voting members present constituted a quorum. She invited those present to address the panel during the Open Public Hearing.

Ms. Nashman read into the record a letter from **Dr. C. H. Rorabeck** of the Division of Orthopedic Surgery from the **University of Western Ontario** urging that cement versus cementless fixation should be considered separately for mobile bearing knees and not in the same context as fixed bearing knees. He noted that clinical experience had been largely with the cemented use of the SAL mobile bearing device mentioned in the petition, that the device is not intended for cementless use, and that there was no experience or data from cementless use of any mobile bearing devices except the DePuy LCS total knee system. He thought the issues relevant to the cement/porous coating distinction are different for fixed and mobile bearing devices, and he urged a graduated device introduction for mobile bearing knees consistent with Class III handling.

Ms. Nashman also read a letter from **Richard W. Parkinson** of the **Wirral Hospital** in the United Kingdom, in which he cited unacceptable clinical results from the

now-obsolete Johnson-Elloy mobile bearing total knee replacement (TKR) and expressed concern that this experience might be repeated if the market is flooded with other designs of mobile bearing TKRs.

The first of four speakers to address the panel on behalf of **DePuy International** was **Steven Peebles**, an employee of **DePuy**, who argued that inclusion of mobile bearing concepts in the reclassification petition was not supported by data.

Dr. Jur Strobos, M.D., a consultant to **DePuy**, argued that the cementless versus cement issues are less important than the mobile bearing knee issues, which have greater impact on public health. After discussing the benefits of Class III classification and the reasons to reclassify a device, Dr. Strobos suggested that cementless or mobile bearing knees are not suitable candidates for reclassification. He discussed the clinical experience with five types of mobile bearing knees, noting the complications and problems found with each design. Dr. Strobos also listed future mobile bearing issues such as femoral component curve, proprietary polyethylene, congruency of bearings, and curve of bearing track. He concluded that design trade-offs are unknown and that mobile bearings are not ripe for reclassification.

Dr. Stephan Leewald, also speaking on behalf of **DePuy**, cited results of a Swedish multi-center survival study comparing the Oxford versus the Marmor knee device in unicompartmental arthroplasty for arthrosis. He found a significant difference in survival in favor of the Marmor knee and said the Oxford knee is not yet suitable for full-scale use. He thought it suitable for limited use only in comparative studies with other unicompartmental knees with known failure rates.

Dr. Fitzpatrick of DePuy International discussed design considerations in MBK prostheses. He listed failure modes such as bearing subluxation, dislocation, fracture, and wear, as well as component loosening. He discussed design evolution and trade-offs, such as acceptable levels of constraint and means of providing it, balance between total fixed and partially fixed joint requirements, and polycentric versus single radius total fixed articulation, concluding that the outcome of such design trade-offs is unpredictable and often unexpected. He analyzed device validation techniques through evaluation of constraints with ASTM F1223, mechanical simulation, analytical simulation, and prospective clinical trials, noting the unsatisfactory results obtained preclinically and the need for prospective clinical validation. He concluded that MBK devices contain trade-offs in significant areas and these trade-offs have no clean solutions. Design developments remain based on clinical experience because no reliable, predictive, preclinical tools exist.

Panel member Dr. Nelson asked the speakers if DePuy has an approved PMA for an MBK and was told that it does. There was a brief discussion of the design differences between the DePuy cemented knee and other knee prostheses. There were no further requests to speak.

Reclassification Petition for Patellofemorotibial Knee

Petitioner Presentation. **Tom Craig** on behalf of **OSMA** presented the reclassification petition for total knee prostheses, which included the cementless tricompartmental total knee, the cementless unicompartmental total knee, and the cemented and cementless mobile bearing total knee. Mr. Craig recapped the history of reclassification of porous hips in February 1992 and discussed the number of knee

surgeries performed annually. He listed risks such as early loosening, metal-backed patella failure, wear, component fracture, bead delamination, dislocation/instability, disassembly of components, and lack of biocompatibility, and showed how design controls, labeling, FDA guidance documents on total knees and modular components, ASTM/ISO standards, QSR requirements, and 510 (k) procedures could address these risks.

Dr. Joshua L. Jacobs discussed cementless, hybrid, and cemented fixation, the mechanics of fixation biology, and retrieval experience. He gave as reasons to use cementless fixation the preservation of bone stock, ease of revision, and durability of fixation. He discussed the bone in-growth phenomenon, and he gave statistics on a retrieval study, noting variability in reasons for removal. He concluded that substantial stability can be obtained regardless of the type and interface and that use or non-use of screws had no effect on stability. Based on his clinical experience with five- to ten-year follow-up data from a prospective, nonrandomized study comparing cemented and cementless fixation, he concluded that the cemented and cementless fixations are essentially equivalent; that cementless is used in a more active patient population, that there is a high failure rate of metal-backed patellar components and high reoperation rates, and that wear, not femoral fixation, is not an issue.

Dr. John J. Insall discussed MBK design rationale and clinical experience. He noted that results with total fixed knee replacement had been good but suggested three reasons to use an MBK knee rather than a fixed knee: polyethylene wear, osteolysis, and kinematics or modularity. He said that the mobile bearing gives a better modularity result because of the high contact area and free rotation, and the polyethylene wear results are

excellent. He acknowledged that problems have been reported but saw no insurmountable problems.

Dr. Robert B. Bourne presented design rationale and clinical experience with the SAL knee. He reviewed the history of TKR and the problems with fixed versus mobile bearing knees. He noted that all MBKs are not the same and suggested that the rotating platform is the best design. He thought the MBK has the advantage of reduced contact stresses and decreased wear. Dr. Bourne suggested post-cruciate preserving or sacrificing as a major consideration in the MBK versus fixed knee decision and cited a nine-year track record of good outcomes with a good range of motion.

FDA Presentation. **Mr. Peter Allen, M.S.**, gave the FDA presentation on the OSMA petition. He read the proposed device description, noting that there are two types of knee prostheses involved, the patello-femoro-tibial metal/polymer/metal/polymer/metal porous coated uncemented articulating prosthesis (total) and the femoro-tibial (unicompartmental) metal/polymer/metal porous coated uncemented articulating prosthesis. He described the femoral component as a cobalt chromium alloy, surface hardened titanium alloy, the tibial components as a polyethylene bearing, cobalt chromium or titanium alloy based, fixed or mobile, and the patella components as a polyethylene bearing, cobalt chromium or titanium alloy based, fixed or mobile. The proposed indications for use included degenerative, post-traumatic, or rheumatoid arthritis and failed osteotomies, unicompartmental or total knee replacement; Mr. Allen noted that the unicompartmental knee is indicated when only one component of the knee is affected.

Mr. Allen outlined the device history, saying that all types require PMAs currently. There are four PMAs approved for uncemented use, two with fixed bearing, one with fixed and mobile bearings, and one with a mobile bearing, unicompartmental. There is one PMA approved for a mobile bearing design with cemented use. Supporting information provided by the petitioner included a bibliography with 300 references in the peer-reviewed literature. These articles covered preclinical issues such as mechanical properties, coating integrity, biocompatibility, and clinical issues. Reviewing the articles, Mr. Allen cited the numbers of unicompartmental and total knee devices of the fixed bearing, uncemented, porous coated type, the mobile bearing, cemented type, and the mobile bearing uncemented, porous coated type and summarized the data as showing that cemented and uncemented knee devices achieve similar pain, complications, and survival results, but uncemented knees take longer recovery time to become pain-free. He listed the risks to health and suggested controls as given in the petition presentation.

Mr. Allen found 652 MDRs reported from 1994 to 1997, of which 532 were device problems. None were listed under product codes for total knees, uncemented, and none under product codes for unicompartmental, uncemented., which he attributed to limitations of the MDR system. Mr. Allen then listed the questions for FDA discussion.

Discussion of Questions and Voting. After some discussion of various possibilities, panel members agreed to the revised classification definition: cemented and cementless but not press-fit unless porous coated, mobile bearing knees with the following characteristics: (1) a mobile platform, polished cobalt chromium/titanium base plate with a minimum 6 to 8 mm disk meniscus, inherent stability in anteroposterior and medial lateral directions for

tibial-femoral articulation, and a mechanism for preventing bearing dislocation; (2) cementless designs with pore size of 100-500 mm, motion of 100 mm, appropriate material (titanium or chromium cobalt) and adequate bone stock. It was felt that the unicompartmental uncemented device should be considered separately, but the risks to health were otherwise adequately described. Most panel members felt that special controls had been adequately identified to address the risks to health, although Dr. Laurencin thought them insufficient for uncemented unicompartmentals. On the risk of metal-backed patella dissociation, four panel members wanted postmarketing surveillance but others felt the controls sufficient. On dislocation and subluxation of mobile bearing components, three suggested postmarketing surveillance, two wanted more information on wear considerations, and the rest thought the controls sufficient. On labeling, Dr. Holeman asked that the indication for use be clarified; others thought the labeling adequate. Panel members unanimously agreed that petition data supported reclassification of patellofemorotibial uncemented porous coated total knee prostheses, but there was no clear consensus on whether sufficient information was presented on femorotibial unicompartmental uncemented porous coated knees. On mobile bearing knees (uncemented and/or cemented), the panel did not think the data as provided in the petition supported reclassification.

The panel completed the general device classification questionnaire for patellofemoral-tibial uncemented porous coated total knee devices, noting that it was not life sustaining or supporting but was of substantial importance in preventing impairment of human health and did not impose an unreasonable risk of injury. There was sufficient

information to establish special controls, which included performance standards and testing guidelines, to provide reasonable assurance of safety and effectiveness. Device availability was restricted to written or oral prescription use only. The panel completed the supplemental data sheet, listing the indications for use and risks to health as those presented in the petition and recommending Class II classification on the basis of adequate data presented in the petition. Standards applicable to the device were listed in the petition. A motion was made, seconded, and carried to accept the worksheets as outlined, thereby recommending Class II classification for patellofemoral-tibial uncemented porous coated total knee devices.

The panel also completed a worksheet and supplemental data sheet recommending Class II classification for femoro-tibial unicompartmental uncemented porous coated fixed bearing knee prostheses. Answers for all questions were the same as those given above, with the exception that special controls such as performance standards, testing guidelines and preclinical studies, and a limited postmarket study involving three or four centers and 30 surgeons to study whether this prosthesis works and remains fixed were recommended. The vote to accept this worksheet to reclassify the femorotibial-tibial unicompartmental uncemented porous coated fixed bearing knee prosthesis to class II was passed by a vote of five to three, with the stipulation on a postmarket study noted. Those who voted against the worksheet and its recommendation (Drs. Nelson, Lavin, and Laurencin) stated that there were insufficient evidence and data for reclassification.

The panel next attempted to fill out a worksheet recommending that tricompartmental mobile bearing cemented knee prostheses with a rotating translating base

be reclassified to class II with special controls of general performance and testing standards (such as ASTM standards). The panel was split on this worksheet, with three members (Drs. Laurencin, Lavin, and Nelson) arguing it set a dangerous precedent for down-classification with limited data. The supplemental data sheet was amended to recommend Class II classification with restrictions on prescription availability, sufficient bone stock, limiting motion to less than 100 microns, and surface of the uncemented stem. When repolled, the panel voted five (Drs. Nelson, Laurencin, Lavin, Aboulafia, and Yaszemski) to three (Drs. Skinner, Besser, and Hill) not to accept the questionnaire recommending reclassification.

The panel then filled out a worksheet and supplemental data sheet on all tricompartmental and unicompartmental mobile bearing knees, both cemented and uncemented, as presented in the original proposal. The panel noted there was not sufficient information to establish special controls to provide reasonable assurance of safety and effectiveness and recommended Class III classification with low priority for requiring premarket approval application submissions. The panel voted overall on the petition as presented that all tricompartmental and unicompartmental mobile bearing knees, cemented and uncemented, should be Class III devices, with the exception of the tricompartmental mobile bearing knee cemented with a rotating translating base, which could be separately considered for reclassification potential to Class II. This recommendation was passed by a vote of five (Drs. Aboulafia, Skinner, Hill, Yaszemski, and Besser) to three (Drs. Laurencin, Nelson, and Lavin).

Petition on Reclassification of Patellofemoral Knee

Petitioner Presentation. **Mr. Mitchell Dhority** began the petitioner presentation on behalf of **OSMA**. He noted that patellofemoral joint arthroplasty is a surgical procedure involving replacement of the femoral trochlear groove and the patella with prosthetic components. It was first performed in 1955 and evolved into patellar and femoral groove replacement in the early 1970s. He discussed its current regulatory situation, noting that its current CFR classification is as a cemented, metal/polymer device of semiconstrained design that is limited to treatment of patellofemoral arthritis or chondromalacia. On the basis of published clinical data and commonality of current designs and controls with TKR devices, the petition sought reclassification to Class II. Clinical results in published literature on a fairly limited patient population indicated good to excellent results in the majority of cases for restoration of range of motion, restoration of quad strength, and pain relief. The most frequent complications cited were sepsis, stiffness and/or pain, patellar tracking problems, failure of device or revision, and involvement of tibial component, which are similar to those in TKR. These risks could be controlled through special controls such as proper patient selection and technique, labeling, design related criteria, and current guidances for 510 (k)s on TKR. The petition recommended reclassification into Class II with minor modification to CFR and control of risks via existing TKR guidelines and applicable regulations.

Dr. Boren presented the rationale and the results of patellofemoral joint arthroplasty studies. He noted that patellofemoral joint arthroplasty alone is more conservative than TKR, and he summarized the history of the procedure. The device consists of a metallic femoral component and polyethylene patellar component. He

outlined the indications for use, which include a patient over age 60, failed patellofemoral surgery, old patellar fracture, patellofemoral osteoarthritis, and chronic patellar dislocation, and he noted that device salvage is relatively easy. Clinical results are based on limit, infrequent use with not much follow-up, but show consistent pain relief, restoration of function, and increasing range of motion. Despite its limited and infrequent use, patellofemoral arthroplasty offers satisfactory results and a more conservative treatment option that can be salvaged to TKR.

FDA Presentation. **Mr. Hany Demian, M.S.**, gave the FDA review of the OSMA reclassification petition for patellofemoral prostheses. He discussed the current Class III classification of the patellofemoral polymer/metal semiconstrained cemented prosthesis for patellofemoral arthritis or chondromalacia and the proposed reclassification for cemented or press-fit prostheses for the same indication. He listed the proposed indications for use (osteoarthritis limited to the distal femur and patella, history of patellar dislocation or fracture, previous surgery with unsatisfactory results). Mr. Demian described the device components as a metal femoral component for cemented or porous coated press-fit and a UHMWPE patella components, including an all-poly patella cemented component or a metal -backed uncemented porous coated component. He summarized the clinical information as five articles on device use and summarized its premarket application history since 1976, with one 510 (k) cleared and three companies currently listed as marketing the device in the United States. He summarized the MDR information since 1985, which consisted of 22 MDRs, the majority of which involved separation of metal backing from the patellar component. He listed the risks to health and

the special controls to address these risks as stated in the petition presentation. He then read the panel questions for discussion.

Questions and Voting. Panel members thought the proposed description was sufficient. The risks to health should include loosening, wear, failure of the metal backing, dislocation, and instability. There was some feeling from a few members that the risks to health for the uncemented prosthesis had not been adequately described, particularly the risk of potential revision. There was consensus that dislocation of the metal backing from the patellar component was not an additional risk beyond those for other metal-backed patellas and that this problem would be addressed by the special controls already listed in the petition. Drs. Nelson, Aboulafia, and Laurencin suggested some clinical follow-up studies could be done on the uncemented prosthesis but not postmarket surveillance studies, which were seen as too diverse. In responding to the FDA questions, the panel initially voted by a narrow margin that there were sufficient prosthesis data presented in the petition to support a reclassification to Class II for both the cemented and uncemented prosthesis, although there was significant disagreement about the uncemented prosthesis.

The panel then filled out a general reclassification questionnaire for the patellofemoral knee prosthesis, uncemented and cemented, recommending reclassification to Class II subject to special controls of performance standards and testing guidelines such as guidance documents. On the supplemental data sheet, labeling additions included listing of the risks to health as potential revision, loosening, wear, dislocation and instability of metal-backed patella, and it was suggested that the labeling information should appear in the brochure rather than the package insert only. The potential for

revision was listed as a risk to health, and the device was recommended for Class II, based on information in the petition. Its availability was restricted to prescription use. A vote was then taken to recommend Class II status for the patellofemoral knee prosthesis, uncemented and cemented, based on information provided in the petition, questionnaire and supplemental data sheet. The motion failed.

Separate questionnaires were then filled out for the patellofemoral cemented and uncemented prostheses. The worksheet on the cemented device was identical to that listed above. A motion was made, seconded, and carried to approve the worksheet recommending to the FDA that the patellofemoral cemented device be reclassified to class II with all the labeling considerations as noted on the worksheets.

The questionnaire on the uncemented patellofemoral device was filled out to state that there is not sufficient information to establish special controls for this device and to recommend Class III classification. The priority for establishing a regulatory performance standard for this device was considered low. On the supplemental data sheet, the indications for use considered were identical to those listed above for the cemented version. The potential for revision was listed as a risk to health presented by the device. It was recommended for Class III classification on the basis of lack of published information on the uncemented prosthesis for this use. A motion to approve these worksheets recommending for Class III classification based on these worksheets was passed by a vote of six to two, with Drs. Hill and Skinner opposing. Dr. Skinner stated his objection to setting a precedent for needing clinical data for porous materials as a method of fixation;

he felt that there was sufficient information from other joint prostheses to warrant Class II reclassification.

Mr. Jim Dillard, Deputy Director of DGRD, asked the panel whether it was saying that it was uncomfortable with approving a class of device because of lack of data on principle, even though enough is known in general about the class from other joints or whether it was uncomfortable about being unable to identify all the risks specific to this class of device because of insufficient data. Dr. Boyan felt that the data probably do exist and the companies should gather such data. It was suggested that clinical data are not necessary in every single circumstance but site-by-site data are variable with porous in-growth, and thus useful. Dr. Skinner reiterated his conviction that there was sufficient information from other joints and that the panel should trust the FDA to make the necessary analysis.

Before leaving as temporary panel chair, Dr. Boyan thanked outgoing Executive Secretary Jodi Nashman for all her work on present and past panel meetings. Dr. Nelson then assumed the position of temporary panel chair for the remainder of the meeting.

Classification Proposal for Calcium Sulfate Bone Void Filler

Sponsor Presentation. Representatives of **Wright Medical Technology, Inc.**, began the presentation on OSTEOSSET calcium sulfate bone void filler. **Dr. Jack Parr** described the device, its composition, and indications for use. He noted that the bone void filler is offered in very small pellets, each consisting of highly purified, medical-grade calcium sulfate or plaster of Paris, with stearic acid as a tableting agent. The pellets are radio-opaque, biocompatible, biodegradable, and resorbable. The device is provided sterile

in vials of 100 or 200 pellets. It is indicated for use in filling bony voids or gaps, whether traumatically or surgically created, that are not intrinsic to the ability of bony structure in the extremities, spine, and pelvis. It may be used alone or in combination with other graft materials. Dr. Parr described the chemical composition and physical as well as chemical characterization methods of the device.

Dr. George Rodeheaver summarized the non-clinical information, detailed the historical research over many years of experimental use of calcium sulfate, and listed experimental observations. He concluded that studies by Dr. Peltier since the 1950s have shown that the inflammatory response to plaster of Paris is no greater than that normally seen at bone repair sites, there is no observable inhibition of osteoblast growth or activity, the device is biocompatible, absorbable, and replaced by histologically normal new bone. In vivo and in vitro studies performed in accordance with the internationally recognized ISO biocompatibility standard have established that the device is biocompatible as an implant in bony tissue. While there were virtually no adverse effects associated with use of plaster of Paris as a bone void filler, it was noted that such filler provides no significant strength or support to the bone structure and that a small, transient elevation of serum calcium has been observed. These results are disclosed in the contraindications against use of the device for structural support or in patients with hypercalcemia. In conclusion he noted that recognized standards and methods promulgated by USP/NF, ASTM, ISO, FDA, and others provide reasonable assurance of safety and effectiveness.

Dr. Steven Gitelis summarized the clinical information, based on 25 published studies of over 500 patients in which plaster of Paris was used alone or in combination

with antiseptic/antibiotic or hydroxylapatite to fill sterile and infected sites under varied conditions. These published observations showed calcium sulfate is well tolerated at the implant site and does not elicit undue tissue reactions, is readily absorbed over a period of weeks, can be used safely in infected sites and does not aggravate the infection, and does not inhibit normal growth or healing of bone. It acts as a scaffold for bone growth until resorption occurs, can be used effectively to extend other graft materials, functions effectively as a vehicle for agents such as antimicrobials and antibiotics without affecting their properties, and is associated with low complication rates. Such complications include infection, drainage, effusion, wound dehiscence, cyst or tumor recurrence, bone fracture, extrusion, implant failure, and lack of osseous in-growth.

Dr. Gitelis also discussed an unpublished prospective study conducted by Wright that is evaluating new bone growth and percent of resorption of the pellets by radiographic analysis. He discussed inclusion and exclusion criteria and preliminary data which show no device-related complications and good bone growth and pellet resorption. He concluded that OSTEOSET and other calcium sulfate bone void fillers can be used effectively in infected sites, can be used effectively with other bone graft materials and agents, and are associated with very low complication rates.

Sponsors concluded by listing potential special controls such as USP/NF monograph requirements for composition and purity; USP, ASTM, and other standard methods for characterization and control of chemical and physical properties; ISO standard recommendations to evaluate biocompatibility; FDA guidance to assess resorption; and labeling disclosures to manage risks to health. Noting two other nearly

identical devices being managed effectively in Class II, they recommended that Class II special and general controls are sufficient to provide assurance of safety and effectiveness.

FDA Presentation. **Ms. Nadine Sloan, M.S.**, gave the FDA review of the proposal. She read the proposed device description, noting modifications on the amount of calcium sulfate used and substance form. She outlined the device's regulatory history, adding that it was the only calcium sulfate bone void filler to be found substantially equivalent to Ethicon's preamendment calcium bone void filler, and that there was a second 510 (k) for the kit version of the device and a third with expanded indications. She read the current indications for use and described the supporting information provided as articles on the preamendment device and results of a prospective clinical study on the Wright pellets. Noting that no MDRs were reported for preamendment or currently marketed devices, she listed the potential risks to health as cyst recurrence, bone fracture, wound complications, transient hypercalcemia, implant fracture, and lack of or incomplete bone growth, and listed the proposed special controls already presented by the sponsor.

Dr. Orlee Panitch reviewed the clinical data, describing the chemistry and the experience from Dr. Peltier's work with plaster of Paris, which consisted of historical information, animal experience, and clinical experience on 20 different patients for various indications. She briefly discussed the design of the prospective study at 10 centers on the current device, summarizing inclusion and exclusion criteria, demographics, diagnosis, and location of defect, and gave statistics on pellet resorption and bone growth and on other graft materials used. In conclusion, she read the USP definition of calcium sulfate and the panel questions.

Panel Review. **Dr. Michael Yaszemski** gave the lead review, in which he observed that the clinical and nonclinical data made sense and posed no compatibility issues. Although he had not personally used the device, he thought the classification proposal reasonable. He noted that the prospective study was still underway and asked if the transient hypercalcemia noted was related to the volume of product used. He also questioned use of the word “scaffold” in the proposal material, noting there are no data on laboratory cell work or in vivo studies. He suggested Class II classification and thought there were adequate special controls listed in the proposal.

Questions and Voting. Discussion concentrated on when adjunctive materials were necessary and on the transient elevation of calcium levels noted in the proposal. Sponsors suggested that adjunctive materials are not necessary in highly vascularized sites but might be useful in non-vascularized beds. They noted that calcium elevation occurred only in the animal studies and should not prevent device use with patients on dialysis, but a contraindication for hypercalcemia was added as a precaution.

In reply to FDA questions, there was panel consensus that the classification description was sufficient and that the risks to health had been adequately characterized, although some members wanted more information on the risk of transient hypercalcemia. It was agreed that special controls were sufficient, with some attention paid to hypercalcemia. It was thought that the appropriate indication for use would be as a bone void filler at surgeon’s discretion with or without adjuncts when OSTEOSSET is not used to provide stability. There was consensus that the indications for use should not specify a maximum defect size and amount of device used.

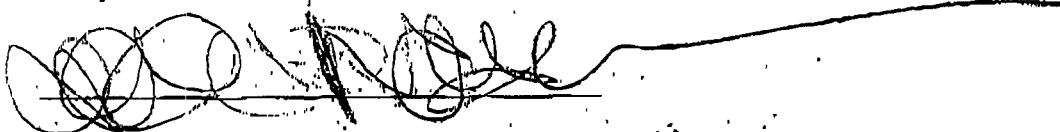
The panel then filled out the general device classification questionnaire, saying that the device was not life-sustaining or supporting, nor was it of substantial importance in preventing impairment of human health. It did not pose an unreasonable risk of potential injury. There was sufficient information to determine that special controls such as testing and voluntary performance guidelines, a small postmarket surveillance for calcium testing, and any other voluntary controls suggested in the proposal would suffice to determine safety and efficacy. The device should be available by prescription only.

The panel then filled out the supplemental data sheet, recommending Class II classification on the basis of information presented in the proposal, with the indications, risks, restrictions, and standards listed therein. A motion was made, seconded, and carried unanimously to accept the worksheets recommending the device for Class II classification.

Executive Secretary Jodi Nashman and Dr. Celia Witten, Director of DGRD, thanked the panel for their assistance. The meeting was adjourned at 5: 15 p.m.

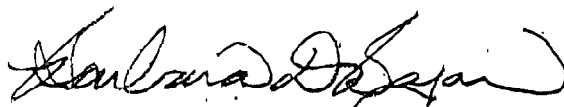
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I certify that I attended the Open Session of the Orthopaedics and Rehabilitation Devices Panel Meeting on January 12-13, 1998, and that this summary accurately reflects what transpired.




Jodi Nashman, M.S., Executive Secretary

I approve the minutes of this meeting as recorded in this summary.



Barbara D. Boyan, Ph.D., Temporary Panel Chair, January 12-13, 1998

I approve the minutes of this meeting as recorded in this summary.



David L. Nelson, M.D., Temporary Panel Chair, January 13, 1998

Summary minutes prepared by

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